Ingestion, Inhalation, and Dermal Exposures to Chloroform and Trichloroethene from Tap Water

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Individuals are exposed to volatile compounds present in tap water by ingestion, inhalation, and dermal absorption. Traditional risk assessments for water often only consider ingestion exposure to toxic chemicals, even though showering has been shown to increase the body burden of certain chemicals due to inhalation exposure and dermal absorption. We collected and analyzed time-series samples of expired alveolar breath to evaluate changes in concentrations of volatile organic compounds being expired, which reflects the rate of change in the bloodstream due to expiration, metabolism, and absorption into tissues. Analysis of chloroform and trichloethene in expired breath, compounds regulated in water, was also used to determine uptake from tap water by each route (inhalation, ingestion, or absorption). Each route of exposure contributed to the total exposure of these compounds from daily water use. Further, the ingestion dose was completely metabolized before entering the bloodstream, whereas the dose from the other routes was dispersed throughout the body. Thus, differences in potential biologically effective doses depend on route, target organ, and whether the contaminant or metabolite is the biologically active agent. *Key words*: chloroform, dermal exposures, drinking water, ingestion exposures, inhalation exposures, trichloroethene, volatile organic compounds. *Environ Health Perspect* 104:48–51 (1996).

Traditional approaches for evaluating exposure to and adverse health effects from contaminants in tap water have assumed that ingestion is the major route of exposure. Thus, when water contamination has occurred, federal guidance documents advised the avoidance of ingestion to protect public health, but did not necessarily warn against other water uses that result in inhalation and dermal exposures, which also increase the body burden of volatile water contaminants (*1*). Furthermore, the ingestion of 2 l of water has been used to estimate the health risk associated with waterborne chemical contaminants and the establishment of drinking water standards (*2*) without quantifying the doses received from other routes. This practice can lead to an underestimation of the potential health risk. Exposure assessment models, pharmacokinetic models, and experimental data measuring breath concentrations of chloroform associated with inhalation exposure and the dermal absorption associated with showering with chlorinated water suggest that inhalation and dermal absorption contribute a measurable dose to the body (*3–7*). These studies predicted that the dose of volatile compounds associated with showering is similar to the dose resulting from ingesting 2 l of water, the exposure upon which regulations are based. Thus, it has been proposed that inhalation and dermal absorption need to be considered in the analysis of total human exposure analysis to volatile contaminants in tap water (*7*).

Metabolism of environmental contaminants occurs in multiple organs, and the site of metabolism is an important determinant of a compound's toxicity. The route of exposure can alter the overall rate and site of metabolism and affect a compound's site-specific toxicity.

The concentration of a volatile compound in exhaled breath is related to its concentration in the bloodstream and can be used to determine changes in body burden with time (*8–10*). Exhaled breath concentrations have also been used to infer the relative internal dose received, the exposure route, and to examine differences in overall metabolic rates (*11–13*).

Physiologically based pharmacokinetic (PBPK) models are used to model the distribution of environmental contaminants and their metabolites in the body (*14,15*). An application of a PBPK model by Blancato and Chiu (*15*) examined the biologically effective dose resulting from exposure to contaminants in water and predicted that for the same amount of internalized chloroform, ingestion exposure results in a higher dose of chloroform to the liver, but inhalation and dermal absorption exposures result in more chloroform being circulated throughout the body and to other organs, such as the bladder. Epidemiological studies examining the health effects of chlorinated water have found that populations exposed to chlorination by-products have elevated bladder cancer rates (*16,17*) and have suggested an association between exposure to chlorination by-products in water and adverse reproductive outcomes (*18,19*).

The present research was conducted to determine the dose of water contaminants resulting from the three common routes associated with water use: ingestion (drinking), inhalation (during showering), and dermal contact (showering, bathing). The results were based on measurements of human breath concentrations of chloroform and trichloroethene following ingestion, inhalation, and dermal exposures to residential tap water. Chloroform is contained in municipal water supplies that are disinfected by chlorination, the most common disinfection process in the United States (*20*). Trichloroethene is a common contaminant in groundwater, particularly near National Priority List or Superfund sites (*21*). To obtain the incremental dose, each experiment was limited to examining a single exposure route.

Methods

Exposure to a single route at a time was accomplished by imposing a control on the routes of exposure not being studied while performing normal activities (drinking, showering, and bathing) (*4*). During an inhalation exposure, the subject wore waterproof clothing while showering to minimize dermal contact. For dermal exposure, the subject breathed purified air while showering or bathing. The compounds were then measured in a time series of exhaled breath samples to monitor their expiration rate.

We performed 25 experiments using 11 subjects (6 males and 5 females between the ages of 20 and 50 years old). Eight 10-min dermal-only "showers" and four 60-min dermal-only baths were taken to evaluate the effect of the dermal exposure route on the elimination rates of volatile organic compounds (VOCs). Nine 10-min inhala-

tion-only showers were taken to evaluate the effect of the inhalation exposure route on elimination rates of VOCs. Four experiments were performed for ingestion of 0.5 l water. Informed consent was obtained from each subject.

Water samples were collected into clean glass vials with teflon-lined enclosures. During collection, care was taken to ensure that no bubbles formed in the water. The water was analyzed for chloroform and trichloroethene by purge and trap followed by GC/MS or GC/electron capture detection (ECD). The air was sampled during the entire inhalation exposure by drawing an air sample through a 0.25-inch ID stainless-steel trap packed with a multilayered, adsorbent trap containing Carboxen 563 (Supelco Co., Belleforte, Pennsylvania), Tenax TA (Alltech Corp., Deerfield, Illinois), and Carbosieve SIII (Supelco). Breath samples were collected using a sampler designed to collect primarily alveolar air (*11*). The subject breathed through a new mouthpiece into a one-way valve that directed the inspired air from a charcoal purifier into the subject and the expired air into a temporary storage tube (0.64 cm × 8 m) from which the breath was continually withdrawn onto an adsorbent trap using a personal sampling pump set at a flow rate of 1 l/min. A series of breath samples were collected after exposure at times ranging from between 1 min and several hours to determine the relative body burden of chloroform or trichloroethene resulting from each exposure. The air and breath samples were analyzed by thermal desorption coupled with GC/MS or GC/ECD. During the inhalation and dermal exposures, the shower and bath water was maintained at a temperature of 40 ± 2°C, a typical water temperature for bathing.

Results and Discussion

Only the breath samples collected seconds to minutes after ingesting residential well water containing trichloroethene had elevated concentrations of trichloroethene. Following ingestion of chlorinated municipal water, none of the breath samples had measurable levels of chloroform. The initial elevation of breath concentrations for trichloroethene is most likely due to off-gassing of VOCs from the residual water present within the oral cavity, rather than reflecting blood–air exchange in the alveolar sacs because no continued elevation was detected. One explanation for this observation is that the internal dose received from ingestion is completely metabolized during a first pass through the liver, thus there was no measurable elevation in VOC concentration in the exhaled breath, which would reflect elevated blood concentrations.

The chloroform and trichloroethene concentrations in the exhaled breath were elevated in each subject after both inhalation and dermal exposures during showering, demonstrating that chemicals in the water entered the body by both routes (Figures 1 and 2). Breath concentrations were also elevated after dermal exposure via bathing (Fig. 1C). In contrast to ingestion, after inhalation and dermal exposure, the exhaled breath had elevated levels for extended time periods, implying that the compounds were distributed throughout the bloodstream before being metabolized. These observations support the predictions of a PBPK model for chloroform exposures from tap water (*15*).

One previous study measured elevated levels of chloroform in blood and breath following a bolus ingestion of 5 x 10⁵ μg (0.5 g) of chloroform (*22*). Our present study used a total ingestion of only 10 μg of chloroform (0.5 l water containing 20 μg/l) and 10 or 20 μg of trichloroethene (0.5 l water containing 20 or 40 μg/l), common environmental levels. The 0.5-g ingestion exposure probably exceeded the metabolic capacity of the liver. Thus, a portion of the chloroform was not metabolized during the first pass through the liver and entered the circulatory system, whereas the ingestion of environmentally relevant concentrations are unlikely to have saturated metabolic enzymes. These data imply that for common environmental levels, if the target organ of a waterborne contaminant is the liver or if a long-lived metabolite is the toxic agent, then an ingestion exposure delivers the largest biologically effective dose via the three routes studied. However, if a different organ is the target, and either the parent compound or a short lived metabolite is the biologically active agent, then inhalation and dermal exposures would deliver a larger biologically effective dose than ingestion. For example, for chloroform, the reactive metabolite phosgene is suspected to be the biological active agent (*23*); thus, inhalation and dermal absorption exposures to chlorinated water will result in a larger chloroform dose and may present a greater risk than ingestion to organs other than the liver, such as the bladder where elevated cancer rates have been suggested (*16,17*), and for adverse reproductive outcomes (*18–20*).

The amount of chloroform expired per microgram of the compound in 1 l of water was calculated from the expired breath profiles, assuming a respiration rate of 0.01 m³/min. These values ranged from 0.02 to 0.05 μg for the inhalation-only exposure (Fig. 1A), from 0.02 to 0.13 μg for the dermal-only shower exposure (Fig. 1B) and
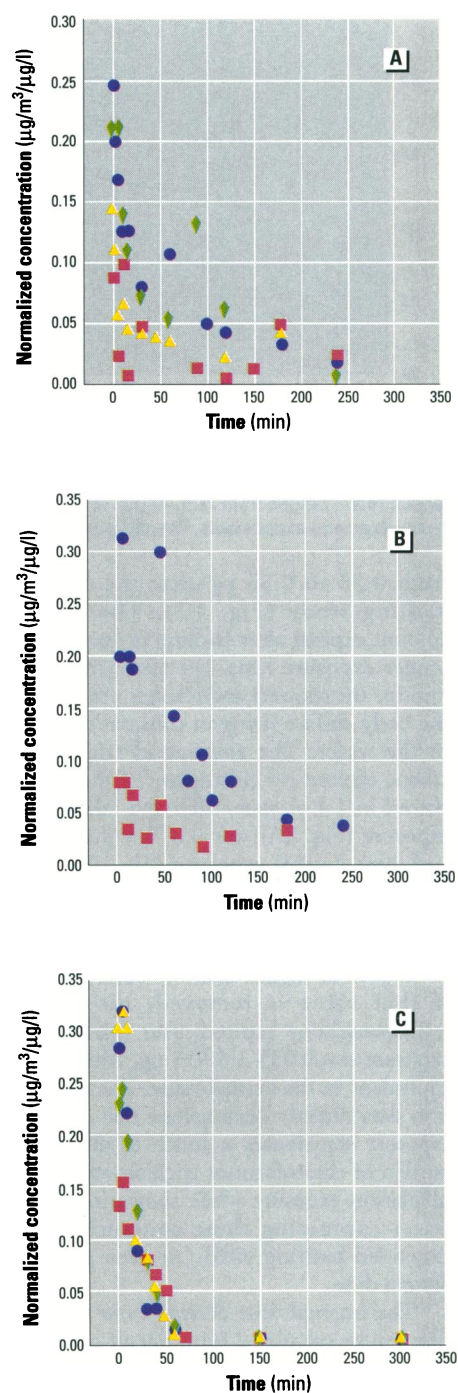
Figure 1. Exhaled chloroform breath time profiles after (A) inhalation exposure during a shower, (B) dermal exposure during a shower, and (C) dermal exposure during a bath. Each symbol represents a different experiment run. The normalized concentration was calculated by dividing the breath concentration by the water concentration. The shower water concentrations ranged from 10 to 50 μg/l for the inhalation exposure experiments and from <10 to 41 μg/l for the dermal exposure experiments; the bath water concentration ranged between 11 and 15 μg/l for the dermal exposure experiments. Four different subjects were used in each shower study; two different subjects participated twice in the bathing study.
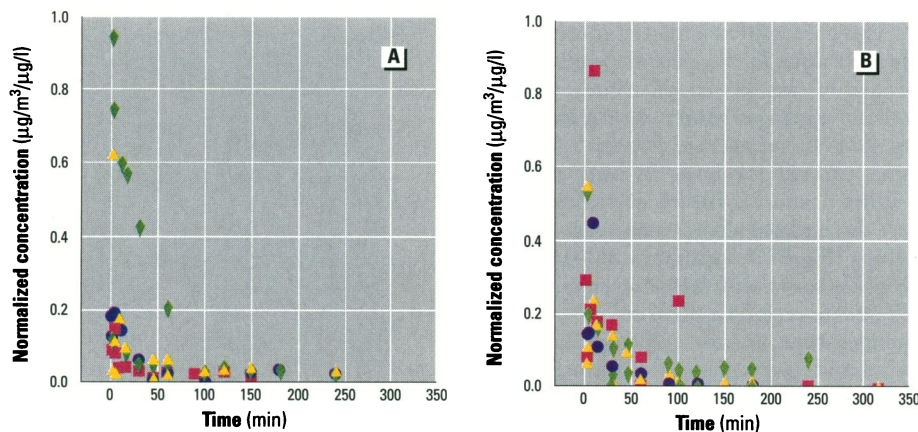
Figure 2. Exhaled trichloroethene breath time profiles after (A) inhalation exposure during a shower and (B) dermal exposure during a shower. Each symbol represents a different experimental run. The water concentration ranged from 28 to 41 µg/l for the inhalation exposure experiments and 16 to 150 µg/l for the dermal exposure experiments. Five different subjects participated.

from 0.33 to 0.56 µg after the dermal bathing study (Fig. 1C). The larger amount expired after bathing is due to the longer exposure time (60 min versus 10 min for the shower) and a larger portion of the body surface being in constant contact in the water. The amount of trichloroethene expired per microgram of the compound in 1 l of water after the inhalation exposure (Fig. 2A) was 0.074 ± 0.080 µg and after dermal exposure (Fig. 2B) was 0.030 ± 0.011 µg. However, the amount of trichloroethene expired after one of the inhalation exposure experiments is an order of magnitude higher than the other values. If that value is removed, the mean trichloroethene expired after inhalation exposure was 0.035 ± 0.018 µg, which was equivalent to the dermal value. The expiration data directly demonstrate that dermal exposure contributes as much to the body burden of chloroform or trichloroethene as inhalation exposure while showering with water containing these contaminants. Extended bathing yields an even greater dermal dose.

The internal dose derived from inhalation can be calculated from the air concentration, breathing rate, duration of the shower, and adsorption efficiency across the lung barrier (9). The calculated internal dose from inhalation exposure ranged between 60 and 250 µg for trichloroethene and between 30 and 80 µg for chloroform. The amount of chloroform and trichloroethene expired after inhalation and dermal shower exposures were similar, suggesting nearly equivalent internal doses for these two exposure routes during showering. An ingestion of 2 l of water containing the concentrations observed in this study and, assuming a 100% transfer across the gastrointestinal tract, yields maximum internal dose estimates for trichloroethene of

30–300 µg and for chloroform of 10– 100 µg. Thus, for typical activities of drinking and showering, each exposure route contributes similar internal doses, and the total internal dose from a 10-min shower or a 30-min bath is greater than that from ingesting 2 l of water.

In conclusion, approximately equivalent amounts of volatile contaminants from water can enter the body by three different exposure routes, inhalation, dermal absorption, and ingestion, for typical daily activities of drinking and bathing. However, the exposure route affects the rates of metabolism and therefore the compound's potential toxicity. The ingested VOCs were metabolized during the first pass through the liver, thus the parent compound was not measurable in the exhaled breath and would not be present in the bloodstream. However, chloroform and trichloroethene concentrations were measurable in the breath after inhalation and dermal exposure, indicating dispersion throughout the body. These results confirm the necessity of knowing the biologically active agent (either the parent compound or a metabolite of VOCs found in water) and the site of activity of a contaminant to accurately quantify the dose received from all significant exposure routes before forming public health policies related to contaminated water supplies.

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